

SEPTEMBER 20, 2006

Hot Topics and News Tips: 2006 HHMI International Scholars Meeting

Howard Hughes Medical Institute (HHMI) international research scholars—some of the world's leading biomedical researchers from outside the United States—will meet at HHMI's new Janelia Farm Research Campus in northern Virginia September 26-29, 2006.

All research is embargoed until the date and time of presentation.

Tips are organized by topic, not chronologically.

Bacterial Battles

Starving Flesh-eating Bacteria Emanuel Hanski, Israel Presentation: 4:35 p.m., Friday, Sept. 29

Streptococcus A causes necrotizing fasciitis, a life-threatening condition commonly called the flesh-eating bacteria infection. Emanuel Hanski, an HHMI international research scholar from Hebrew University, Hadassah Medical School in Jerusalem, Israel, has identified a protein from the *Strep A* bacteria that prevents the cells of the immune system from fighting the infection in the skin. Hanski is working on a new treatment strategy for this dangerous infection that involves taking the bacterial protein out of action by reducing the production of a key enzyme, ScpC, either by finding an inhibitor of the enzyme or by finding a way to boost production of another protein called SilCR that counters its activity.

Hanski is publishing a paper on this approach in the October 4, 2006, issue of *EMBO Journal*.

Beating Antibiotic-resistant Bacteria Natalie Strynadka, Canada Presentation: 9:15 a.m., Wednesday, Sept. 27

Natalie Strynadka, an HHMI international research scholar from the University of British Columbia in Vancouver, Canada, has determined the structure of a protein that Gram-negative bacteria, such as *Staphylococcus aureus*, need to survive. She has found that a mutant form of that protein

prevents normal antibiotics from binding to and killing the bacterial cell. Strynadka is using her background in understanding protein structure, which she has gained as a crystallographer, to design new antibiotics that bind to the mutant form of the *Staph* protein. The new drugs appear to be highly effective in killing multiple drug-resistant strains of *Staphylococcus aureus*. Strynadka was recently elected to the prestigious Royal Society of Canada.

Taming Anthrax Diego de Mendoza, Argentina Presentation: 8:25 a.m., Thursday, Sept. 28

Gram-positive bacteria, such as the bacteria that cause anthrax, are a global health problem and potential bioterrorism threat. Diego de Mendoza, an Argentine HHMI international research scholar, is an expert in the field of lipid metabolism in Gram-positive bacteria. He has discovered a protein that regulates the activity of many of the genes involved in lipid metabolism. Proper lipid metabolism is essential for survival of the bacteria. He also identified an enzyme that helps maintain the integrity of the bacterial cell wall. His discoveries are expected to provide unique targets for more effective treatments of Gram-positive bacterial infections. De Mendoza is director of the Institute of Molecular and Cellular Biology of Rosario, National Council for Scientific and Technical Research (CONICET), in Argentina.

Why TB Is Hard to Kill Valerie Mizrahi, South Africa Presentation: 9:15 a.m., Wednesday, Sept. 27

A new drug-resistant strain of tuberculosis (TB) has hit South Africa, killing more than 50 people already. HHMI international research scholar Valerie Mizrahi, South Africa's woman scientist of the year, is on the front lines of this emerging epidemic. Since her research focuses on the molecular mechanisms underlying drug-resistant TB, Mizrahi has a unique vantage point from which to provide expert commentary on this health threat. She is a professor at the University of the Witwatersrand Medical School in Johannesburg, and co-director of a new South African Department of Science and Technology Centre of Excellence for Biomedical TB Research. Mizrahi is widely recognized for her mentoring of South African science students.

***E. Coli's* Salad Days** B. Brett Finlay, Canada Presentation: 11:25 a.m., Thursday, Sept. 28

More and more people are falling prey to *E. coli* infection from tainted spinach. *E. coli* experts like B. Brett Finlay, an HHMI international research scholar at the University of British Columbia in Canada, can explain how the *E. coli* bacteria place a death grip on intestinal cells. Finlay's lab determined the molecular structure of *E. coli*, information that could aid in development of a vaccine for humans, as well as a vaccine for cattle, because *E. coli* often is transmitted by ground beef. Finlay has been an HHMI international research scholar since the Institute's first competition for Canadian and Latin

American scientists in 1991. In 2003, *Time* magazine named him one of Canada's top five scientists to have influenced health worldwide. Finlay recently won the Flavelle Medal, the Royal Society of Canada's highest honor.

Tiny Conspiracies: Cell-to-Cell Communication in Bacteria Bonnie Bassler, USA Keynote address: 6:30 p.m., Wednesday, Sept. 27

While a chattering crowd of various species of bacteria is essentially a microbial tower of Babel, certain snippets of their chemical conversation are almost universally understood by other bacteria. Bonnie Bassler, who studies how bacteria communicate with each other, has found that bacteria of different species can talk to each other using a common language—and that some species of bacteria can manipulate the conversation to confuse other bacteria. This interspecies crosstalk and misdirection could have important consequences for human health, says Bassler, an HHMI investigator at Princeton University. She will describe her research on quorum sensing, which is the production, release, and detection of signaling molecules that enable bacteria to regulate gene expression. Bassler also will talk about research focusing on developing therapies that interfere with quorum sensing, to control bacterial virulence.

Bugs, Drugs, and Microarrays Joseph DeRisi, USA Keynote address: noon, Friday, Sept. 29

As a graduate student, Joseph DeRisi, an HHMI investigator at the University of California, San Francisco, helped invent and pioneer the use of DNA microarray technology. As an established researcher, he now moves readily among disciplines, shares what he knows as widely as possible, and dives fearlessly into new scientific challenges. He uses that same approach to study the activity of the full range of malaria genes and emerging viral diseases, including a new retrovirus in humans that is closely related to a cancer-causing virus found in mice. At the HHMI international research scholars meeting, DeRisi will discuss his accelerated malaria drug discovery program and the viral diagnostic and virus discovery system he has developed. This system has helped DeRisi and his colleagues identify a novel viral pathogen that may be implicated in prostate cancer.

Promising Parasite Research

Love Songs of the Sand Fly Siblings Alexandre Peixoto, Brazil
Presentation: 5:25 p.m., Friday, Sept. 29

In Central and South America, the tiny, blood-sucking sand fly spreads a parasite that causes visceral leishmaniasis, a disease that is often fatal if untreated. Brazilian HHMI international research scholar Alexandre Peixoto studies the genetics of behavior in these flies. He has found that sand fly males produce a love song during copulation and that different populations

have very distinct songs that are influenced by the expression of specific genes. This indicates that the main vector of visceral leishmaniasis in Brazil is in fact four or more sibling species of sand fly, a result confirmed by analysis of love-song genes. Because sibling species often differ in their potential for spreading disease, these findings could have important implications for leishmaniasis control. Peixoto is a researcher in the Department of Biochemistry and Molecular Biology at the Oswaldo Cruz Foundation in Rio de Janeiro.

Winning the War Against Malaria:

Sumalee Kamchonwongpaisan, Thailand Presentation: 8:50 a.m., Friday, Sept. 29

Malaria, caused by the parasite *Plasmodium falciparum*, infects 300 to 500 million people annually and kills up to 3 million, most of them children. Thai HHMI international research scholar Sumalee Kamchonwongpaisan studies the molecular targets of two new antimalarial drugs: derivatives of artemisinin—one of the most effective antimalarial drugs—and antifolate drugs that interfere with synthesis of DNA and other essential components of the malaria parasite. Her findings could lead to the development of more effective strategies to contain this global threat. She is a researcher at the National Center for Genetic Engineering and Biotechnology in Pathumthani, Thailand. In 2003, she received the Taguchi Prize for outstanding research achievements by a young scientist in the field of biotechnology.

Brendan Crabb, Australia Presentation: 10:10 a.m., Friday, Sept. 29

Surface proteins from the malaria parasite are promising candidates for use in a malaria vaccine because they may help generate a robust immune response. HHMI international research scholar Brendan Crabb, a chief of laboratory at the Walter and Eliza Hall Institute of Medical Research, in Melbourne, Australia, has identified a number of previously unrecognized surface proteins that are displayed by the parasite when it invades red blood cells. These proteins may play an important role in the parasite's movement from host cells and its invasion of red blood cells.

Robert Ménard, France Presentation: 10:35 a.m., Wednesday, Sept. 27

Once a mosquito bite has jabbed the malaria parasite through the skin of its host, the parasite can interact with host cells in two ways: It can move through the cell, a process known as cell transversal, or it can infect the cell by invading and developing in a vacuole, a tiny compartment inside the cell. Robert Ménard, an HHMI international scholar and a chief of laboratory at the Pasteur Institute of Paris, has determined that cell traversal actually may mask cell infection of the host's liver cells. Knowing this offers a new target for disrupting the life cycle of the malaria parasite.

Neuroscience News

Marijuana's Cousins: New Anti-anxiety Drug? Tamás Freund, Hungary
Presentation: 1:25 p.m., Wednesday, Sept. 27

Millions of people suffer from anxiety disorders. Tamás Freund is a Hungarian neuroscientist and HHMI international research scholar who studies the brain circuitry that links learning and emotions. When these networks malfunction, mood disorders—particularly anxiety—can result. Freund has discovered how endocannabinoids, or marijuana-like compounds that occur naturally in the brain, regulate responses of nerve cells in these brain circuits. Understanding this mechanism provides potential targets for new drugs to treat anxiety disorders. Freund is director of the Institute of Experimental Medicine, Hungarian Academy of Sciences in Budapest, Hungary.

Talk to the Scientists

Scientists from Russia and Israel will be available during the meeting to talk with reporters about their experiences doing scientific research in their countries.

What's Happening to Science in Russia? Maria Garber and Mikhail Gelfand, Russia

After the fall of the Soviet Union, Russian scientists were left to scramble for scarce funding, equipment, and supplies. Russia has gone through many changes since then, but the fundamental problems remain: funding, lack of scientific infrastructure, bureaucracy, little scientific collaboration with the West, and the ongoing brain drain.

Maria Garber, chief of the Laboratory for Structural Studies of the Translational Apparatus at the Institute of Protein Research, Russian Academy of Sciences, Pushchino, has been an HHMI international research scholar since the Institute's first competition for scientists in the former Soviet Union in 1995. Mikhail Gelfand is chief of laboratory at the Institute for Information Transmission Problems, Russian Academy of Sciences, in Moscow. In 2004, he received one of three prizes awarded to "Best Scientist (Doctors of Science, Biology)" from the Russian Academy of Sciences.

Garber and Gelfand can offer reporters personal accounts of the state of science and scientific research in Russia today.

Research in a War Zone Shulamit Michaeli and Emanuel Hanski, Israel

The recent conflict between Israel and Hezbollah in Lebanon made a normally tense situation that much worse for Israeli scientists. Shulamit Michaeli and Emanuel Hanski, HHMI international research scholars from

Israel, have watched their graduate students and postdoctoral fellows leave the lab to join the military, not knowing when or if they would return. "Sometimes they phone from the tanks to check up on their research," says Michaeli. "Our lab is a family. I concentrated on the science and tried not to think about the bombings." Both Michaeli and Hanski have had to sleep in their labs for fear of going out on the street.

Michaeli is a microbiologist at Bar-Ilan University in Israel. She studies parasitic trypanosomes that cause Chagas disease and sleeping sickness. Hanski, a professor at Hebrew University's Hadassah Medical School in Jerusalem, studies invasive strains of group A streptococcus, the bacteria that cause necrotizing fasciitis, also known as flesh-eating bacteria. Both are willing to share their experiences of trying to conduct scientific research during a war.